

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
21 December 2000 (21.12.2000)

PCT

(10) International Publication Number
WO 00/76309 A2

(51) International Patent Classification⁷: **A01K 67/027**

(21) International Application Number: **PCT/EP00/05318**

(22) International Filing Date: 8 June 2000 (08.06.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
99201859.8 10 June 1999 (10.06.1999) EP

(71) Applicant (for all designated States except US):
VLAAMS INTERUNIVERSITAIR INSTITUUT VOOR BIOTECHNOLOGIE VZW [BE/BE]; Rijvisschestraat 120, B-9052 Zwijnaarde (BE).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **CARMELIET, Peter [BE/BE]**; Sappelenbos 10, B-3052 Blanden (BE). **COLLEN, Désiré [BE/BE]**; Schoonzichtlaan 20, B-3020 Winksele (BE). **DAHLBACK, Bjorn [SE/SE]**; Regementsgatan 8, S-211 42 Malmo (SE). **GARCIA DE FRUTOS, Pablo [ES/ES]**; Rios Rosas 41, Flat 3-1, E-08006 Barcelona (ES). **APARICIO, Cristina [ES/ES]**; Rios Rosas 41, Flat 3-1, E-08006 Barcelona (ES).

(74) Agent: **BRANTS, Johan, Philippe, Emile; De Clercq, Brants & Partners cv, E. Gevaertdreef 10 a, B-9830 Sint-Martens-Latem (BE).**

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

— Without international search report and to be republished upon receipt of that report.

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 00/76309 A2

(54) Title: NON-HUMAN TRANSGENIC ANIMALS DEFICIENT IN GAS6 FUNCTION AND THEIR USE

(57) Abstract: It has been shown that Gas6 deficient endothelial cells are resistant to activation by endotoxin and TNF- α *in vitro* and *in vivo* and that leukocytes did not or much less extravasate in Gas6 deficient mice. The present invention also relates to the manufacture of a medicament for the treatment of endothelial dysfunction. The present invention further relates to the use of an inhibitor of the Gas6 function and/or an inhibitor of a Gas6 receptor for the manufacture of said medicament.